

Interview Summary

Application No.

09/762,304

Applicant(s)

MEYER-ALMES, FRANZ
JOSEF

Examiner

MISOOK YU, Ph.D.

Art Unit

1642

All participants (applicant, applicant's representative, PTO personnel):

(1) MISOOK YU, Ph.D.

(3) _____

(2) Debby Huynh

(4) _____

Date of Interview: 12 May 2003

Type: a) ☒ Telephonic b) ☐ Video Conference

c) ☐ Personal [copy given to: 1) ☐ applicant 2) ☐ applicant's representative]

Exhibit shown or demonstration conducted: d) ☒ Yes e) ☐ No.

If Yes, brief description: FAX (attached)

Claim(s) discussed: N/A

Identification of prior art discussed: N/A

Agreement with respect to the claims f) ☐ was reached. g) ☐ was not reached. h) ☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: Ms Huynh from Clontech stated that Clontech began selling the caspase assay kits with slight different name beginning in 1997.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

Examiner's signature, if required

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record

A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews

Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,
- 2) an identification of the claims discussed,
- 3) an identification of the specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner,
(The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
- 6) a general indication of any other pertinent matters discussed, and
- 7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

BD Biosciences

Clontech
1020 East Meadow Circle
Palo Alto, CA 94303-4230
toll free: 877.232.8995
tel: 650.424.8222
fax: 650.424.1352
www.bdbiosciences.com



May 12, 2003

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Miss Yu
US Patent Office
703-308-2454 (ph)
703-746-7647 (fax)

Dear Miss Yu:

Here are the catalog pages from 1997 and 1998 for our product number K2026-1.

Let me know if I can help you out in any other way.

Regards,



Debbie Huynh
Director of Customer Support
BD Biosciences Clontech
877-232-8995 option 5, ext 1112
dahuynh@clontech.com

1997/1998

catalog

- Assay one of the earliest proteases associated with apoptosis
- Quick, quantitative assay performed on cell lysates
- Easily formatted for a microtiter plate

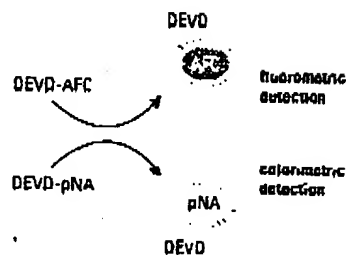


Figure 14.4. Fluorometric and colorimetric detection of CPP32 protease activity. Fluorometric detection is performed at 505 nm, and colorimetric detection is performed at 405 nm.

Fluorometric and colorimetric kits based on the detection of molecules cleaved from ICE-family protease substrates. The ApoAlert CPP32 Fluorescent Assay Kit detects the shift in fluorescence emission of 7-amino-4-trifluoromethyl coumarin (AFC). The AFC-substrate conjugate, DEVD-AFC, emits blue light ($\lambda_{max} = 400$ nm); however, upon proteolytic cleavage of the substrate by CPP32, free AFC emits a yellow-green fluorescence at 505 nm. Similarly, the ApoAlert Colorimetric Assay Kit is based on spectrophotometric detection of the chromophore *p*-nitroanilide (pNA) after cleavage from the labeled substrate DEVD-pNA. Comparison of the fluorescence of AFC or absorbance of pNA from an apoptotic sample with an uninduced control allows determination of the fold increase in protease activity. The protease activity can also be accurately quantified using a standard curve established with the appropriate free fluorescent or chromogenic molecule.

The ICE-family proteases (caspases) initiate cell death by degrading specific structural, regulatory, and DNA repair proteins (1, 2); CPP32 is responsible for the cleavage of several such substrates. Thus, in many systems, CPP32 protease activity can be used to detect apoptosis earlier than any other assay (4, 7).

Unlike some assays that require purified protein, the CPP32 Protease Assay Kits use crude cell lysates that can be prepared from as few as 10^6 suspension or adherent cells. The cells are resuspended and lysed on ice. The assay consists of adding reaction buffer and the appropriate substrate, incubating for one hour, and analyzing the samples in a fluorometer or spectrophotometer. Either detection method can also be used with a microtiter plate reader.

The CPP32 Kits offer a low-cost, quantitative assay without the need for expensive equipment and they permit detection of apoptosis using a spectrophotometer. CLONTECH also offers a number of apoptosis-inducing reagents and ICE-family protease inhibitors (see page 103).

STORAGE CONDITIONS: -20°C

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Product	Size	Cat. #	Price
ApoAlert CPP32 Fluorescent Assay Kit	25 assays 100 assays	K2026-1 K2026-2	\$121.00 \$368.00
ApoAlert CPP32 Colorimetric Assay Kit	25 assays 100 assays	K2027-1 K2027-2	\$121.00 \$368.00

COMPONENTS

- Cell Lysis Buffer
- 2X Reaction Buffer
- DTT
- CPP32 Fluorescent or Chromogenic Substrate (DEVD-AFC or DEVD-pNA)
- Free Fluorophore or Chromophore (AFC or pNA)
- CPP32 Inhibitor, DEVD-FMK
- Complete User Manual (PT5083-1)

REFERENCES

1. Lazebnik, Y. A., et al. (1993) *Nature* 371, 740-742
2. Casaccia-Reno, L., et al. (1994) *J. Biol. Chem.* 269, 30757-30760
3. Fernandez-Moncha, I., et al. (1994) *J. Biol. Chem.* 269, 30761-30764
4. Casaccia-Reno, L., et al. (1994) *J. Exp. Med.* 180, 1957-1964

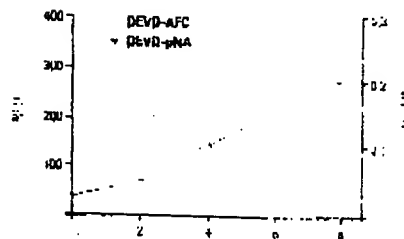


Figure 14.5. Onset of CPP32 activity after induction of apoptosis. 32D cells grown with 2.5 ng/ml IL-3 were treated with 100 μM etoposide (VP-16) at 37°C for the indicated times. Cells were then harvested and lysates were incubated with the indicated CPP32 substrate as described in the ApoAlert CPP32 Protease Assay Kit User Manual. Samples were read in a microtiter plate-reading fluorometer with a 360-nm excitation filter, 508-nm emission filter, and gain setting of 48, or in a spectrophotometer at 405 nm. RFU = relative light units, RFU = relative fluorescence units.

TECHNICAL SUPPORT • FAX 800-424-1350 OR 415-424-1064 TEL 800-662-CLON (2566) OR 415-424-8222
MAIL tech@clontech.com INTERNET <http://www.clontech.com>

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1998/1999 Catalog

ApoAlert™ Caspase Assay Kits

DETECT CPP32 OR FLICE PROTEASE ACTIVITY

- Measure one of the earliest indicators of apoptosis
- Convenient, quantitative fluorometric or colorimetric assay
- Performed directly on cell lysates
- Easily formatted for high-throughput applications

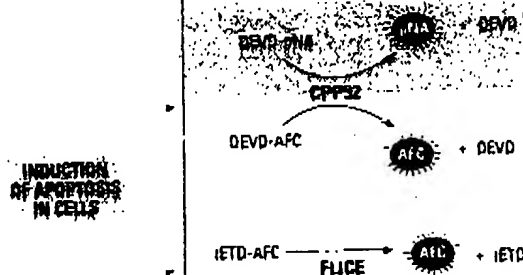


Figure 9.2. Detection of caspase activity during apoptosis. Top panel: Active CPP32 protease cleaves DEVD substrates. The CPP32 Assay is available in both colorimetric (shaded area) and fluorometric (white area) formats. Bottom panel: Active FLICE protease cleaves the IETD substrate. The FLICE assay is available in a fluorometric format. AFC conjugates are used for fluorometric detection of protease activity at 505 nm. pNA conjugates are used for colorimetric detection at 405 nm.

Fluorometric and colorimetric kits based on the detection of molecules cleaved from substrates of caspase proteases (ICE-family proteases). These proteases initiate apoptosis by degrading specific structural, regulatory, and DNA repair proteins within the target cell (1, 2). FLICE/Caspase-8 is the putative initiator of the caspase pathway, directly or indirectly activating CPP32 and other caspases (3, 4). CPP32/Caspase-3 is responsible for the actual degradation of several vital cellular proteins. Because caspases act so early in apoptosis, these kits can detect apoptotic activity in an induced cell population sooner than other assays (5).

The ApoAlert CPP32/Caspase-3 and FLICE/Caspase-8 Fluorescent Assay Kits detect the shift in the fluorescence emission of 7-amino-4-trifluoromethyl coumarin (AFC) AFC is conjugated to a specific tetrapeptide sequence—DEVD for the CPP32 Kit, IETD for the FLICE Kit. Normally the conjugate emits blue light. Upon cleavage of the substrate by protease, the liberated AFC emits a yellow-green fluorescence at 505 nm. Fluorescence detection is highly sensitive and can be used to measure even minute amounts of active caspase.

The ApoAlert CPP32/Caspase-3 Colorimetric Assay Kit measures the proteolytic cleavage of the chromophore p-nitroanilide (pNA) from a DEVD tetrapeptide sequence. Liberated pNA can be detected rapidly and conveniently in any standard spectrophotometer at 405 nm.

Assays are performed directly on crude cell lysates from 10^4 suspension or adherent cells. Multiple samples can be measured in a microtiter plate for high-throughput analysis.

All the caspase kits provide a low-cost, quantitative assay that does not require expensive equipment. In addition to these three kits, CLONTECH also offers a number of apoptosis-inducing reagents and caspase inhibitors (pages 77–78).

STORAGE CONDITIONS: -20°C

CLONTECH

Received from < 800 424 1350 > at 5/12/03 4:30:38 PM [Eastern Daylight Time]

Product	Size	Cat. #	Price
ApoAlert CPP32/Caspase-3 Fluorescent Assay Kit	25 assays 100 assays	K2028-1 K2028-2	\$127.00 \$386.00
ApoAlert CPP32/Caspase-3 Colorimetric Assay Kit	25 assays 100 assays	K2027-1 K2027-2	\$127.00 \$386.00
ApoAlert FLICE/Caspase-8 Fluorescent Assay Kit	25 assays 100 assays	K2028-1 K2028-2	\$127.00 \$386.00

APOALERT CPP32/CASPASE-3 ASSAY KIT COMPONENTS

- Cell Lysis Buffer
- 2X Reaction Buffer
- DTT
- CPP32 Fluorescent or Chromogenic Substrate (DEVD-AFC or DEVD-pNA)
- CPP32 Inhibitor, DEVD-CHO
- Free fluorophore or chromophore (AFC or pNA)
- Complete User Manual (P13083-1)

APOALERT FLICE/CASPASE-8 FLUORESCENT ASSAY KIT COMPONENTS

- Cell Lysis Buffer
- 2X Reaction Buffer
- DTT
- FLICE Substrate, IETD-AFC
- FLICE Inhibitor, IETD-CHO
- Free AFC
- Complete User Manual (P13191-1)

REFERENCES

1. Lazebnik, T. A., et al. (1993) *Nature* 371:546–547
2. Casaccia-Reno, L., et al. (1994) *J Biol Chem* 269:30757–30760
3. Mischak, H. M., et al. (1994) *Proc Natl Acad Sci USA* 91:14466–14471
4. Mischak, H., et al. (1997) *J Biol Chem* 272:24512–24516
5. Casaccia-Reno, L., et al. (1994) *J Exp Med* 180:1957–1964

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